

NATIONAL MARROW DONOR PROGRAM®

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Grant Award N00014-05-1-0310

QUARTERLY
PERFORMANCE / TECHNICAL REPORT
For the Period
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Office of Naval Research

And

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14. ABSTRACT Task 1 : Evaluate optimal short term storage parameters for stimulated and unstimulated leukapheresis (donor lymphocytes) and bone marrow products, including the type of storage media and the cell concentration, in addition to temperature and duration of storage before processing or infusion. Task 2: The NMDP has developed an algorithm that "predicts" high resolution HLA typing results on donor samples that exist in the Registry with only low or intermediate results reported. Perform validation of the NMDP algorithm by selecting donors randomly from our Registry that have low or intermediate DRB1 typing results and using the algorithm to predict the high resolution results and test the ability of the algorithm to predict KIR ligand mismatching in the absence of existing HLA-C locus results.					
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National Marrow Donor Program® N00014-05-1-0310
HLA Typing for Bone Marrow Transplantation
Progress Report for the Period 7 Funding
October 1, 2006 – December 31, 2006

Task 1: Product Validation

Description:

The objective of this study is to evaluate optimal short term storage parameters for stimulated and unstimulated leukapheresis (donor lymphocytes) and bone marrow products, including the type of storage media and the cell concentration, in addition to temperature and duration of storage before processing or infusion.

Project 1. Effects of Media Storage and Cell Concentration

Stimulated and unstimulated leukapheresis and bone marrow products that are representative of products collected and provided for NMDP transplant patients will be purchased. Aliquots of the product will be stored in different storage media at varying cell concentrations per mL of media. Standard graft characterization parameters will be tested.

Objectives:

1. Transportation factors: Determine the effects of different types of tissue media, nucleated cell concentration on CD34+ cell, CD3+ and total nucleated cell viability, and CFU-GM frequency during transport from collection sites to the transplant centers.
2. Overnight storage factors: Determine the effects of different type of tissue media, type of storage bags (gas permeable or non gas permeable), nucleated cell concentration on CD34+, CD3+ cell and total nucleated cell viability, and CFU-GM frequency during overnight storage.

Project 2. Effects of Time and Temperature

Stimulated and unstimulated leukapheresis and bone marrow products that are representative of products collected and provided for NMDP transplant patients will be purchased. Aliquots of the product will be stored at varying lengths of time and temperature. Standard graft characterization parameters will be tested.

Objectives:

1. Temperature factors: Determine the optimal short term storage temperature to preserve nucleated cell count, percent viable TNC, CD34+ and CD3+ cells, CFU-GM frequency and sterility.
2. Time factors: Determine the effect of time on nucleated cell count, percent viable TNC, CD34+ and CD3+ cells, CFU-GM frequency and sterility.

Activity:

The Product Validation study was initiated. The period of performance is set to be complete during the next Quarter (February 2nd, 2007). The project laboratory encountered delays due to IRB review and approval requirements and then availability of study subjects during the December holiday season. Consequently the project is currently behind timeline. Efforts were made to adjust the product recruitment and testing timeline. Testing was completed on three unstimulated PBMC and two mobilized PBSC. The remaining products; 1 unstimulated PBMC, 2 mobilized PBSC and 5 marrow samples will be tested and the project completed in the next quarter.

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Task 2: Validation of the Expectation – Maximization (EM) Algorithm

Description:

The NMDP has developed an algorithm that “predicts” high resolution HLA typing results on donor samples that exist in the Registry with only low or intermediate results reported. A modified version of this algorithm predicts HLA results at loci where there are no typings based on existing typings at other loci and the ethnic-specific haplotype frequencies observed in the population.

It is our intention to incorporate this logic into the mechanisms used to select matched donors for patient searches. Incorporation of this logic would improve the specificity of donors that appear on patient’s searches, which then decreases the costs and time necessary to identify the optimally matched donor. This logic will also be used to provide estimates of the likelihood of finding matched donors in the Registry including matching at loci where some donors in the Registry do not currently have typings.

A portion of the funding would be used to assist in the validation of the NMDP algorithm by selecting donors randomly from our Registry who have low or intermediate DRB1 typing results and using the algorithm to predict the high resolution results. The HLA typing results would be used to validate the accuracy of this method in an unbiased data set.

The remaining portion of the funding would be used to test the ability of the algorithm to predict KIR ligand mismatching in the absence of existing HLA-C locus results. Randomly selected donors from the Registry without HLA-C would be run through a modified version of the algorithm to predict the C locus KIR ligand status. The HLA intermediate resolution typing would validate the accuracy of this method in an unbiased data set.

A laboratory would perform the high resolution HLA-DRB1 testing and/or intermediate resolution HLA-B and C from stored samples of the donors. Quality control and performance criteria will be monitored by a Scientific Services Specialist. The results will be analyzed by a programmer in the Bioinformatics group to verify the accuracy of each prediction technique.

In addition to assisting with the validation of the algorithm, this typing project has potential to impact subsequent patient searches simply due to the increased level of resolution for the Registry donors whose typings have been upgraded. A portion of this typing may be selected on behalf of searching patients in order to further validate the approach and provide direct positive impact on these searches.

Activity:

This Task was completed in a previous period.